THE EFFECT OF CERTAIN HYPERKINEMICS ON THE BLOOD FLOW THROUGH THE SKIN* **

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The general public, judging by sales figures, is making wide use of skin irritating ointments and liniments because of their rubefacient qualities whereas the medical profession, primarily because of the absence of concrete evidence of therapeutic value, has failed to attribute much value to them. This medical opinion may be justifiable because such skin irritants have not been shown to be sufficiently efficacious in the treatment of those conditions for which they are recommended and no serious attempt has been made to assay the relative effectiveness of the various products available. This study has a dual objective, to evolve a reliable method for the evaluation of the effectiveness of the different preparations by estimating the increase in blood flow and to apply such a method towards the different preparations available on the market. It is furthermore of interest to note how deep the effect of such so-called "counterirritants" is on underlying structures. In our search for means to produce an increased blood flow in limbs with spastic or organic occlusive vascular disease an evaluation of "counterirritants" seemed very much in place. In previous communications (1, 2) we were able to demonstrate that radon, in an ointment base, when applied to the skin produces long lasting hyperemia, markedly increased capillary permeability and is resorbed through the intact skin into the blood stream. If some of the simpler "rubefacients" were able to produce similar relatively long lasting effects, their abandonment as therapeutic adjuvants would not be justifiable.

Friedeman (3) was able to show that in an area where blood flow and capillary permeability were increased by chemical means, several times the amount of an intracutaneously injected toxin is neutralized by intravenously injected antitoxin as compared with an untreated control spot. Besides the more rapid removal of toxins and metabolites, "rubefacients" which at the same time lead to an increase in skin temperature, should also lead to a vasodilatation in the underlying structures. In addition, reflex vasodilation in the area of the reflex arc may produce vasodilation in deeper layers. The work of Wood and Weisman (4), Hewlett (5), and Taylor (6) shows, however, that some rubefacients, as for example mustard and turpentine do not produce an increase in skin temperature in spite of the production of a definite outspoken redness of the skin. The vasodilation in these cases seems to be mainly venous in character, thus not producing an increase in blood flow through the area. It is thus evident that a simple estimation of the redness of an anointed area does not necessarily give a true picture of the increase in blood supply. The term rubefacients is therefore

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** Supported by a grant from the Standard Laboratories Inc.

Received for publication September 13, 1948.

ambiguous as to its physiologic basis. Passive and active hyperemia are both included in it although physiologically and therapeutically there is a great difference between the two. We, therefore, suggest the use of the term "hyperkinemics" for preparations which increase the blood flow through an area.

In order to test the efficiency of commonly used hyperkinemics, six preparations were bought on the open market, of which five are old remedies while the sixth has only just appeared. The qualitative composition of the active ingredients of the preparations is shown in table 1. Since some manufacturers have refused to give an exact quantitative analysis of their products, we have refrained from giving the quantitative figures for all of them. We were also unable to obtain an exact description of the ointment carriers used, although these are probably of great importance in the total effects.

TABLE 1

Qualitative composition of different counterirritants

1	2	3	4	5	6
Oil of Mustard Camphor Menthol	Wormwood Thymol Menthol Acetone	Extractum capsicum Methyl salicylate Oil of camphor Oil of pine Turpentine	Methyl salicylate Menthol Baume Analgesique	Oil of mustard Methyl salicylate Menthol Camphor	Oleoresin capsicum Methyl salicylate Oil of white camphor Oil of pine Menthol Eucalyptus Turpentine

METHOD

Both arms of each volunteer used in this study were exposed for 15 minutes to room temperature which varied between 70° and 76°F in all experiments but not more than 2°F in each individual experiment.

On the outer aspect of the upper arms of each volunteer seven circular areas of 2″ diameter were outlined by marking the circumference with a line produced by a 1% alcoholic iodine solution. After the lapse of 15 minutes, basic skin temperature readings were taken with an iron-constantan thermocouple which was recalibrated before each set of readings. Subsequently each of the marked areas was covered with one of the preparations, leaving one area untouched for readings of changes in the basic skin temperature. The ointments were applied with a spatula in a thickness of approximately 1 mm. while the liquid preparations were applied with a sponge of absorbent cotton until the area was completely and amply covered and the excess running over the outlined borders was removed by wiping with absorbent cotton. The skin temperature was read at 4 minute intervals for the first 20 minutes and at 10 minute intervals from then on for the first hour. Thereafter, readings were taken every 15 minutes for the second hour and every 30 minutes thereafter. The area of application of the

different preparations was rotated counter-clockwise from experiment to experiment to eliminate possible errors due to constant hyper- or hyposensitivity of a certain region of the arm. The values noted were corrected for the variation in temperature which the untreated test spot underwent from reading to reading.

Thirty-five volunteers, 20 male and 15 female, between the ages of 16 years and 62 years were thus examined. Thirty-three subjects were white and two colored. In 25 of them the test was carried out for 120 minutes while in ten others it was continued for a total time of 270 minutes.

RESULTS

Of the six preparations thus investigated, preparation number 1 (Fig. 1) showed a marked *lowering* of the skin temperature for the average duration of 75 minutes. The greatest decrease in temperature was on the average 4.25°C and occurred 10 minutes after the application. A slight increase in skin temperature up to a maximum of 1.5°C started 130 minutes after the application. The

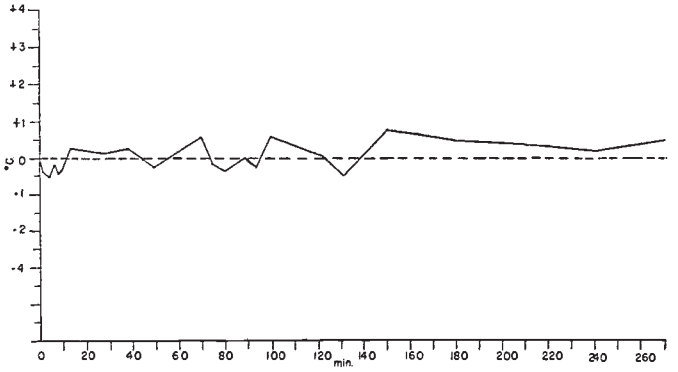

FIG. 1

area under the curve drawn from the average of the readings taken on all volunteers represents the effectiveness of the preparation as documented by the rise in skin temperature in relation to time after application. It is expressed in degree-minutes. For preparation 1 this value is −20.0 degree-minutes. It is thus evident that on the average this preparation does not increase the blood flow through the area to which it is applied.

Preparation number 2 shows a maximal rise of skin temperature of 0.75°C, 110 minutes after application and the value of degree-minutes of the average curve was found to be 55.05 degree-minutes (Fig. 2). This value is very low and does not indicate any appreciable increase in blood flow through the area as would be documented by a considerable rise in skin temperature.

Preparation number 3 shows a rise of temperature of 0.75°C on the average after 15 minutes and a maximum rise in skin temperature of 1°C after 210 minutes. The area under the curve expressed in degree-minutes is 96.56 (Fig. 3). The increase in blood flow producing this rise starts to be worthwhile mentioning although it still is rather low compared with certain other compounds.

Preparation number 4 shows a rise in temperature of 1°C after 15 minutes and continues to rise to a maximum of 2.75°C after 270 minutes. The area under the

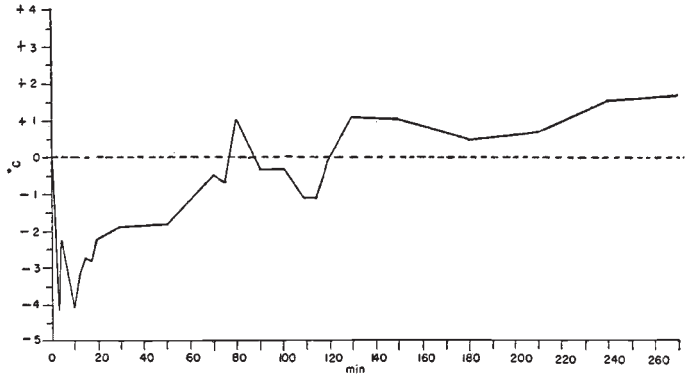

FIG. 2

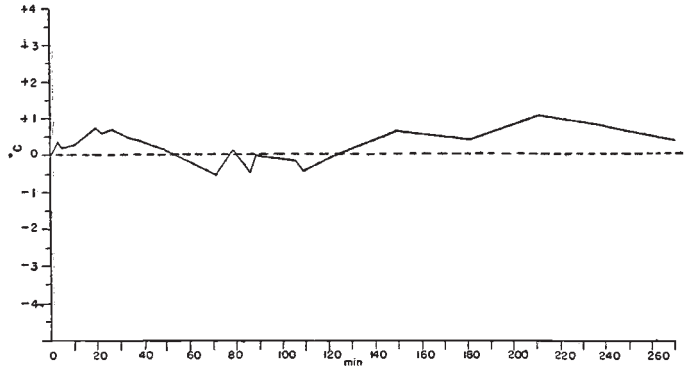

FIG. 3

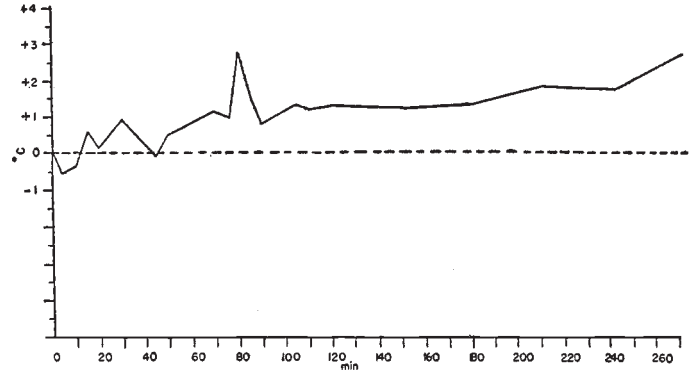

FIG. 4

average curve is 329.98 degree-minutes, a value which documents a considerable increase of blood flow through the test spot (Fig. 4).

Preparation number 5 shows a rise of 2.5°C after 20 minutes and a maximum of 4.25°C after 70 minutes. Thereafter, however, the rise of temperature decreases markedly. The area under the curve is 569.01 degree-minutes indicating a remarkable increase in blood flow (Fig. 5).

Preparation number 6* increases the average skin temperature by 3.25°C in 40 minutes and reached a maximum of 5.5 degrees increase after 70 minutes. It is noticeable that this increase is maintained approximately throughout the entire length of the test, i.e. through 270 minutes. We know from scattered observations that in some of these cases such a rise in temperature was maintained

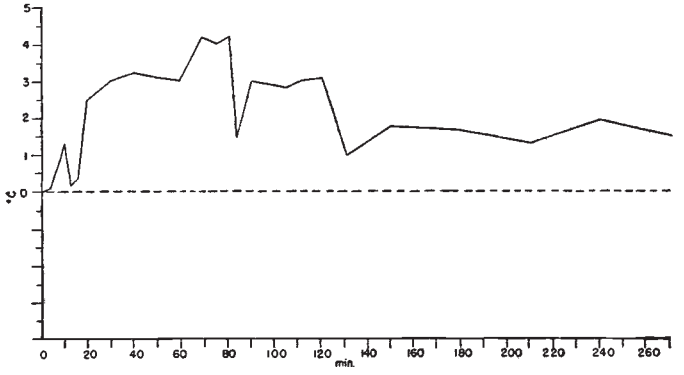

FIG. 5

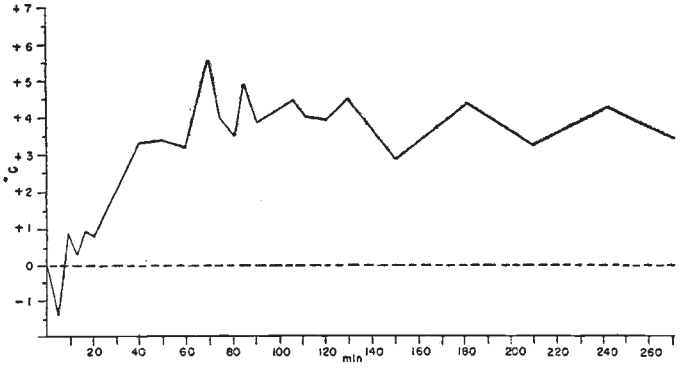

FIG. 6

for another 90 minutes after the termination of the test. The area under the curve is 832.63 degree-minutes which documents a most remarkable and long lasting increase in blood flow through the area (Fig. 6).

All data were submitted to statistical analysis and the differences between the various preparations were found to be statistically significant.

In order to test the depth to which the increase in temperature extends under the skin, thermoneedles were inserted subcutaneously in three volunteers. The

* This preparation was first supplied by the Standard Laboratories and later on was bought on the open market.

depth of the sensitive part of the needle was 0.5, 2.6 and 4.0 cm. respectively under skin level. Needles were applied simultaneously on the flexor surface of both upper arms but the ointment was applied on one side only to be able to correct for spontaneous variations in temperature. Preparation number 6 was applied to the skin above the needle. It turned out that on such an application there is a considerable increase in temperature 0.5 cm. below the skin, somewhat less at 2.5 cm. below the skin and none 4 cm. below the surface (Fig. 7). It must be mentioned, however, that at a depth of 4 cm. the basic temperature is practically identical with the rectal temperature and it is thus hard to imagine how it possibly could increase by vasodilatation. This may be different in the presence of a diminished blood flow in cases of vasospasm.

It is thus evident that from six of the better known hyperkinemics at least three show but a slight increase in blood flow when tested by skin temperature readings. Three others, however, produce increasing degrees of hyperemia in

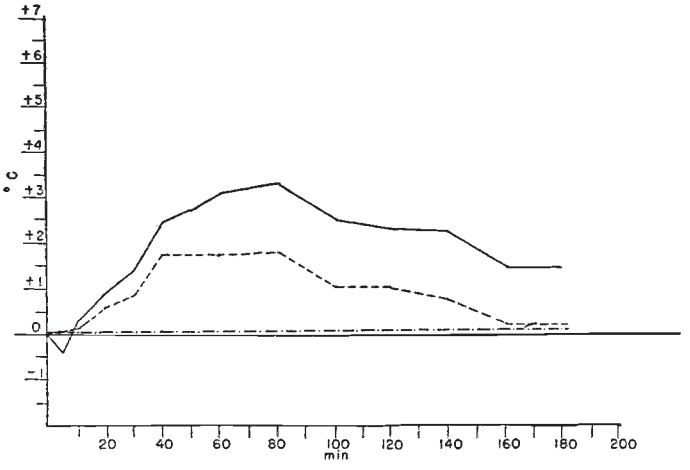

FIG. 7

the area where they were applied to an extent which seems to warrant more widespread use in conditions where a long standing active local hyperemia is desirable. Preparation number 6 showed a longstanding and very marked increase in blood flow which lasted for at least 4½ hours and probably much longer.

It was interesting to note in each of the preparations tested that the pattern of response was rather uniform from individual to individual, but that the general sensitivity to hyperkinemics as such varied greatly in different persons.

It has not been the aim of this investigation to determine which chemical compound is most effective in producing hyperkinemia and which vehicle would be the best to produce such an effect. We rather attempted to evaluate available and widely used available "counterirritants" in their efficacy. It was found that there is a wide difference between different preparations being offered for this purpose, the effects ranging from complete ineffectiveness to a fairly good increase in blood flow through the treated area.

SUMMARY

1) The term rubefacients does not distinguish between substances which produce active or passive hyperemia. It is therefore suggested that the term hyperkinemics be used for compounds which produce an increased flow of blood through an area.

2) Hyperkinemics can be of real therapeutic value by producing a considerable increase in skin temperature and capillary permeability, leading to a better blood supply of an area and to the faster removal of metabolites and toxins.

3) Six commercially available rubefacients were tested on 35 volunteers for their ability to produce an increase in skin temperature as measured by thermocouples. Products vary in ability to increase blood flow.

4) Three preparations failed almost completely to increase the skin temperature, one even reduced the skin temperature slightly. One was only very slightly effective.

The other three preparations produced a temperature increase but in different degrees. One preparation was found to be highly effective but decreased in effectiveness towards the end of the test period of $4\frac{1}{2}$ hours. One preparation was very effective as well as long lasting in effectiveness without decrease towards the longest test periods of $4\frac{1}{2}$ hours.

The sensitivity for hyperkinemics varies greatly in different individuals but the general pattern of reaction to the different preparations is rather constant in different persons. The effect of a superficially applied hyperkinemic can extend to the depth of 2.5 cm. below skin surface as measured by thermoneedles.

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